



## Migraine; clinical and electroencephalography findings in children

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### ABSTRACT

**Aim:** Migraine is a clinical entity that occasionally represents a diagnostic problem. An apparent history and clinical manifestation of migraine may mask the epileptic attack accompanying migraine. The aim of this study is to present our experience with clinical and electroencephalography (EEG) findings and treatment of our patients diagnosed with childhood migraine disease.

**Methods:** We documented six patients who were initially followed-up with a diagnosis of migraine, subsequently observed to have epileptic seizures, and then diagnosed with migraine.

**Result:** Our patients became asymptomatic by giving good responses to antiepileptic therapy based on clinical and electroencephalography (EEG) findings.

**Conclusions:** This case series shows that EEG recording can be useful in all stages of migraine for long-term, safe monitoring. Identifying patients with possible migraine will enable them to receive antiepileptic treatment.

**Keywords:** Epilepsy; migraine; migraine; children.

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Received 2018-11-26, Revisions 2018-12-13

Accepted 2018-12-17

Publication Date 2019-01-01

### Introduction

The term migraine derives from a combination of the words migraine and epilepsy [1]. The condition is defined as a

migraine-triggered seizure [2]. The relationship between the two clinical conditions is a complex one.

Migraine is not included in the classification of epilepsy while taking part in headache classification. According to ICHD-III beta 1.5.5, migraine constitutes a seizure triggered by a migraine aura [3]. ICHD-III diagnostic criteria for migraine are as follows: A, a seizure meeting diagnostic criteria for one type of epileptic attack, B, occurring in a patient with 1.2 migraine with aura, and during or within 1 hour of an attack

of migraine with aura, C. not better accounted for by another diagnosis[1].

The prevalence of migraine among epilepsy patients is 7-26%, while that of epilepsy among migraine patients is 1-17% [4,5]. In both cases there is evidence to support the hypothesis that migraine and epilepsy are comorbid states. A common underlying mechanism has been suspected, because many patients have been observed to experience seizures and headaches. Mitochondrial diseases, especially MELAS (Mitochondrial Myopathy, Encephalopathy, Lactic Acidosis and Stroke-like episodes) and mitochondrial DNA polymerase gene (POLG1) mutations, can present with both epilepsy and migraine. In MELAS, the posterior cerebral region is affected in patients with epilepsy, while POLG1 mutations cause the occipital lobe to be affected. Damage in these areas may cause migraine to develop [6,7]. Another mechanism, cortical spreading depression (CSD), was first proposed by Lashley in 1941 [2,3]. Release of glutamate by glial cells was recognized as triggering CSD in the 1970s [8]. Although the mechanism and spread of CSD is not yet fully understood, hyper-excitability and synchronicity are regarded as the common basic mechanism in epilepsy and migraine. Seizure discharges in the occipital lobes are assumed to trigger an actual migraine headache through CSD without other associated cortical epileptic signals, leading to the activation of the trigeminovascular system or brainstem mechanisms, as previously described [9].

The term migralepsy was introduced by Lennox & Lennox (1960) to describe a condition in which “ophthalmic migraine (= migraine with aura) is followed by symptoms characteristic of epilepsy” [8]. Since then, there have been only 60-70 reports of cases of

migralepsy [4,10,11]. Most of these involved adult patients. The aim of this study is to present our experience with clinical and electroencephalography (EEG) findings and treatment of our patients diagnosed with childhood migralepsy disease.

## Methods

We evaluated the clinical and EEG findings of six patients diagnosed with migralepsy based on migraine ICD-III beta criteria in the pediatric neurology clinic between January 2015 and August 18. Clinical and EEG findings were obtained from patients' hospital records. Patients with a history of seizures during migraine attacks were included in the study. Patients with migraine or epilepsy only, with ictal epileptic headache or with postictal headache were excluded. In addition, brain magnetic resonance imaging (MRI) findings of all patients were also obtained. Ethics committee approval for the study was obtained from Bolu Abant Izzet Baysal University Clinical Research Ethics Committee (No. 2018/129). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

## Results

Our patient data are shown in Table 1. Four of our patients were girls (9-16 years) and two were boys (aged 10 and 14 years). All patients had epileptic seizures with migraine headaches without aura. Two patients had a family history of epilepsy (patients 1 and 4), and two had a family history of migraine (patients 2 and 3).

All patients responded poorly to classic migraine treatment (flunarizine, propranolol etc.).

Physical & neurological examinations (including ophthalmological examination) and hematological and biochemical laboratory findings were normal. Since EEG video-monitoring is not available in our clinic, we performed interictal EEGs, which were either abnormal or epileptiform (Table 1 and Figure 1). MRI of the brain was normal in all patients. Patients with migraine and epileptic seizures were evaluated for migralepsy, and antiepileptic treatment was initiated.

Clinical and EEG responses to antiepileptic treatment were very good. Our patients are still being monitored after one to four years.

## Discussion

Migralepsy was first described by Lennox & Lennox [1,2,8]. Migraine with aura was reported in three cases, involving focal seizure in one and generalized seizure in two in the aura period [12]. These presentations then continued as case series [13,17].

Epileptic attacks were accompanied by migraine aura or headache periods in these studies [13]. EEG findings exhibit variations in migralepsy cases and series in the literature.

Anderman et al reported eight cases with generalized tonic clonic seizures during the aura period; two cases of interictal EEG were normal, the others exhibiting spike and sharp wave activities in the T (temporal) and O (occipital) regions [12]. Niedermeyer and et al

**Table 1.** Age, sex, and clinical and EEG findings of the migralepsy patients

| Patient | Sex/Age | Family history (migraine or epilepsy) | Seizure type | Symptoms (during migraine)                | Interictal EEG  | Follow-up time | Treatment     |
|---------|---------|---------------------------------------|--------------|---|---|----------------|---------------|
| 1       | F/10    | Yes                                   | GTC          | Nausea<br>Photo/<br>phonophobia           | BiFC sharp waves                                      | 3 years        | Oxcarbazepine |
| 2       | M/10    | Yes                                   | GTC          | Nausea vomiting<br>Photo/<br>phonophobia  | Left FC rhythmic sharp waves, generalized spike waves | 21 months      | Valproic acid |
| 3       | M/14    | Yes                                   | Focal        | Nausea, vomiting<br>Photo/<br>phonophobia | BiFCT sharp and slow waves                            | 4 years        | Valproic acid |
| 4       | F/12    | Yes                                   | Focal        | Nausea, vomiting<br>Photo/<br>phonophobia | BiCT sharp and slow waves                             | 9 months       | Oxcarbazepine |
| 5       | F/16    | No                                    | GTC          | Nausea, vomiting<br>Photo/<br>phonophobia | generalized multiple spike wave complex               | 27 months      | Valproic acid |
| 6       | F/9     | No                                    | GTC          | Nausea, vomiting<br>Photo/<br>phonophobia | generalized spike/sharp/multiple spike slow waves     | 10 month       | Valproic acid |

reported eight cases of generalized tonic clonic seizures in the migraine aura period regarded as possible migralepsy [14]. In another study, 13 cases, mostly with focal convulsions in the migraine aura period, exhibited abnormal ictal and interictal EEGs [15]. In one study, periodic lateralized epileptiform discharges were mainly seen on ictal EEGs in seven cases with focal feature seizures [16]. Migralepsy cases occur as migraine aura-induced seizures in adult patients [16]. A four-year-old with emotional stress-induced migralepsy was described in one report [11]. Most cases in the literature consist of adult patients with migraine with aura. Rarely, there are cases of migralepsy diagnosed as migraine without aura [14,17,18].

**Figure 1.** EEG of patient 2 showing generalize multiple spike-wave activity and burst pattern occurring in stage II sleep.



As seen in the previous literature and in our patients, migralepsy is a clinical entity that sometimes poses a diagnostic problem. A distinct history of migraine and its clinical manifestation may mask the accompanying epileptic episode. Headache may have an aura, ictal pattern or be a postictal sign of epileptic seizures. Re-evaluation of patients who do not respond well to migraine treatment and EEG recording may be considered. Diagnosis of migralepsy may be delayed until manifest epileptic seizures occur in these patients.

Our patients were diagnosed with migraine and did not respond well to treatment. Epileptic seizures occurring during follow-up suggested a diagnosis of migralepsy, which we confirmed with EEGs. The most important characteristic feature of our patients was migralepsy without aura. Cases of migralepsy without aura have also been reported previously [14,17,18].

The two most important limitations of our study are that diagnosis of migralepsy was not supported by video EEG monitoring, and the low number of cases. Future large series studies might perform video EEG recording in patients with migraine, including symptomatic and asymptomatic headache processes. This will make it possible to document the potential epileptic character of all stages of migraine.

To summarize, in the light of previous reports and our own cases; i) migraine should be very carefully differentiated from all other neurological paroxysmal disorders, including epileptic seizure, ii) EEG recording can be useful for long-term safe monitoring in all stages of migraine, iii) abnormal or epileptiform EEG records may also be valuable in terms of the possibility of migralepsy, and iv) migraine patients who do not respond sufficiently to treatment may perhaps be suitable for antiepileptic therapy treatment if indicated by the EEG findings.

**Acknowledgements:** We would like to thank to the patients and their families for their perseverance and kind cooperation.

**Informed Consent:** Written informed consent was obtained from the patients who participated in this study.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Funding sources:** The financial support of our work was supported by the Istanbul University Scientific Research Projects Unit (BAP).

## References

- [1]Kasteleijn-Nolst Trenite D, Parisi P. Migraine in the borderland of epilepsy: "migralepsy" an overlapping syndrome of children and adults? *Epilepsia*. 2012; 53 Suppl 7: 20-25.
- [2]Crepeau AZ. Migralepsy: a borderland of wavy lines. *Curr Neurol Neurosci Rep*. 2014; 14(2): 427.
- [3]Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;33(9):629-808.
- [4]Parisi P. Who's still afraid of the link between headache and epilepsy? Some reactions to and reflections on the article by Marte Helene Bjørk and co-workers. *J Headache Pain*. 2009;10(5):327-29.
- [5]Gameleira FT, Ataíde L, Raposo MC. Relations between epileptic seizures and headaches. *Seizure*. 2013; 22(8): 622-26.
- [6]Klopstock T, May A, Seibel P, Papagiannuli E, Diener HC, Reichmann H. Mitochondrial DNA in migraine with aura. *Neurology*. 1996; 46(6): 1735-38.
- [7]Engelsen BA, Tzoulis C, Karlsen B, Lillebø A, Laegreid LM, Aasly J, et al. POLG1 mutations cause a syndromic epilepsy with occipital lobe predilection. *Brain*. 2008; 131 (Pt 3): 818-28.
- [8]Larrosa B, Pastor J, López-Aguado L, Herreras O. A role for glutamate and glia in the fast network oscillations preceding spreading depression. *Neuroscience*. 2006;141(2): 1057-68.
- [9]Kasteleijn-Nolst Trenité D, Parisi P. Migraine in the borderland of epilepsy: "Migralepsy" an overlapping syndrome of children and adults? *Epilepsia* 2012; 53: 20-25.
- [10]Labate A, Sturniolo M, Pucci F, Quattrone A, Gambardella A. Migraine attack triggering a generalised seizure: is this a case of migralepsy or ictal epileptic headache? *Neurol Sci*. 2012;33(4):957-59.
- [11]Tozzi E, Marrelli A. Migralepsy: A Case Report. *Int Neuropsychiatric Dis J*. 2017; 10(2): 1-6.
- [12]Sances G, Guaschino E, Perucca P, Allena M, Ghiotto N, Manni R. Migralepsy: A call for a revision of the definition. *Epilepsia*. 2009; 50(11): 2487–96.
- [13]Basser LS. The relation of migraine and epilepsy. *Brain*. 1969; 92: 285-300.
- [14]Niedermeyer E. Migraine-triggered epilepsy. *Clin Electroencephalogr*. 1993; 24(1): 37–43.
- [15]Marks DA, Ehrenberg BL. Migraine-related seizures in adults with epilepsy, with EEG correlation. *Neurology*. 1993; 43(12): 2476–83.
- [16]Velioglu SK, Ozmenoglu M. Migraine-related seizures in an epileptic population. *Cephalalgia*. 1999; 19(9): 797–801.
- [17]Maggioni F, Mampreso E, Ruffatti S, Viaro F, Lunardelli V, Zanchin G. Migralepsy: is the current definition too narrow? *Headache* 2008; 48(7):1129–32.
- [18]Friedenberg S, Dodick DW. Migraine-associated seizure: a case of reversible MRI abnormalities and persistent nondominant hemisphere syndrome. *Headache*. 2000; 40(6): 487–90.